REMARKS

1. General Matters

1.1. A new title, six words in length, has been provided, which is based on the preamble of claim 1.

1.2. We have deleted the extraneous "of" in claim 1, line 2. The "of" in line 3 is not extraneous, it is the beginning of the prepositional phrase "of a ghrelin-like compound..." which explains what has been administered. Deleting it would result in an ungrammatical sentence.

1.3. We thank the Examiner for rejoining claims 33-35. With regard to the merits of the holding of *a posteriori* lack of unity over Bednarek, see section 5 below.

2. Definiteness (OA §§6-8)

2.1. We have deleted the "such as..." clause in claim 1 and 39 and the term "preferably" in claim 39.

While the Examiner's criticism of the "such as" clause in claims 1 and 39 is appropriate, we note that at the end of OA §6, the Examiner treats clause (b) as if it were part of the "such as" clause at the end of (a). That is improper. The correct interpretation of clauses (a) and (b) is discussed below.

2.2. In OA §8, the Examiner says that claims 1 and 39 are improper because the stated ranges for m (1-10) and n (0-35) are such that it is possible to choose values of m and n which are inconsistent with clause (a), requiring a length of 27-28 amino acids.

We must first note that the claim does not require that the compound satisfy clause (a). Rather, what it actually requires is that the compound satisfy either (or both) of clauses (a) or (b). If the compound satisfies (b), the length limitation of (a) is irrelevant.

Directing our attention first to the compounds of (a), we would say that the Examiner is looking at matters the wrong way.

The definition of m and n are not "inconsistent" with clause (a). Rather clause (a) imposes a constraint on the choices of m and n if clause (a) applies.

In our formula, Z^1 and Z^2 are protective groups, and X^2 is a single amino acid. So if clause (a) applies, and the peptide is therefor 27-28 amino acids in length, m + n must equal 26 or 27 amino acids. Since m is at least 1, n cannot then be greater than 26. And since m cannot exceed 10, n must then be at least 16.

Clause (b) requires at least 90% homology with ghrelin, which is natively 28 amino acids.

Clause (b) does not impose an explicit size limitation but we need to consider whether one is implicit in the % homology language. The specification states, "the software matches similar sequences by assigning degrees of homology to various substitutions, deletions and other modifications". Page 47, lines 21-22. The implication is that a deletion (a gap in the query sequence relative to the reference sequence) reduces the degree of homology. There is language at lines 16-17 which exempts insertions, but it says nothing of deletions. So we consider the 90% homology to impose an implicit minimum length. 90% of 28 is 25.2. A fractional amino acid is meaningless, so clause (b) requires m+n+1 to be at least 26.

However, the specification states that "Neither N- or C-terminal extensions nor insertions shall be considered as reducing identity or homology". Hence the peptide may include additional amino acids, causing m+n+1 to exceed 28, without reducing the % identity.

What, then, is the effect of (b) on m and n? If m=1 (minimum value), n must be 25 to 35. If m=10 (maximum value), n must be 15 to 35. (In contrast, clause (a) permitted n to range from 16 to 26.)

Thus, considering the length implications of alternatives

(a) and (b), m can be any value from 1 to 10, and n can be any value from 15 to 35.

We have amended claim 1 to recite that the minimum value for n is 15 but we don't believe any further amendment of m and n is appropriate even though the choices of, say, m=1 and n=1 would be inconsistent with (a) and (b).

It is not indefinite for a claim to recite ranges for different constituents simply because some nominal combinations of the allowed numbers are impossible, or inconsistent with other limitations. Thus, In re Kroeckel, 504 F.2d 1143, 183 USPQ 610 (CCPA 1974) held that it was acceptable to recite a composition consisting of

A 20-80%

B 20-80%

C 12-25%

even though the claim could in theory read on an impossible composition in which constituents A, B and C added up to more than 100%. MPEP 2172.05(c)(II) cited this decision, with apparent approval, and it seems quite analogous to the situation which would exist here if clause (a) were mandatory and not merely one of two alternatives. Since clause (b) is available as an alternative, there is even less reason to reject here than there was in Kroeckel.

3. Written Description

The Examiner asserts that claims 1-2, 6, 14-20, 22-23, 27-29, 31, 33-35, 37, 39, 40 and 43-44 fail to comply with the written description requirement.

By implication, the Examiner admits that examined claim 3 (ghelin-like compound at least 98% homologous to SEQ ID NO:1) and claim 13 (ghrelin, SEQ ID NO:1) do satisfy written description. (Somewhat inconsistently, the Examiner rejects claim 14 even though they are directed to the completely disclosed sequences

SEQ ID NOs:1-3.)

Claim 1 is a generic claim which recites a ghrelin-like compound which comprises a structure defined by formula I

$Z^1-(X^1)_m-(X^2)-(X^3)_n-Z^2$

wherein Z^1 and Z^2 are optional protecting groups; X^1, X^2 and X^3 are independently chosen amino acids, and X^2 is in particular an amino acid "modified with a bulky hydrophobic group"; m is 1-10; and n is 0-35.

These are all subject to the further constraint that

(a) said ghrelin-like compound or pharmaceutically acceptable salt thereof is 27-28 amino acids in length, with the proviso that said ghrelin-like compound is at least 80 % homologous to SEQ ID NO 1, and/or

(b) said ghrelin-like compound is at least 90 % homologous to SEQ ID NO 1,

According to MPEP 2163(II)(A)(3)(a)(ii), for a claim drawn to a genus, written description exists if there is a sufficient description of a representative number of species by (1) actual reduction to practice, (2) reduction to drawings or structural chemical formulas, or (3) disclosure of a sufficient combination of identifying characteristics.

In the original sequence listing, pp. 117-119 of the specification, there is clearly disclosure of complete structures for the following sequences:

(1) SEQ ID NO:1, 28 a.a., human ghrelin, Ser-3 is modified with fatty acid;

(2) SEQ ID NO:2, 27 a.a., differs from SID 1 by deletion of Q14;

(3) SEQ ID NO:3, 28 a.a., rat ghrelin, differs from SID 1 by mutations K11R, A12V, and is thus 26/28 or almost 93% homologous to SID 1.

We also disclose various truncated peptides on pages 40-43.

Applicants also set forth specific preferred $(X^1)_m$ sequences at P38, L25-29, preferred X2 at page 39, lines 7-10, preferred $(X^1)_m$-(X^2) sequences at lines 11-15; preferred (X^3) sequences at page 38, lines 21-27 and page 39, line 10 to page 43, line 26.

We thus have disclosed, by complete structure, the sequences of at least three compounds which are within the scope of the generic claim (and we have disclosed several potentially relevant partial structures).

We begin by considering whether the complete sequences are "representative" of the claimed genus. The Examiner has questioned (1) whether there is a sufficient disclosure of a correlation between function and structure of compounds beyond those explicitly disclosed and (2) whether there is sufficient variety of species to reflect the variance in the genus.

The Examiner's attention is respectfully directed to the Written Description Training Materials, Example 14. This said that reduction to practice of a single sequence ("SEQ ID NO:3") was sufficient to establish written description of a claim directed to "a protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A→B". The PTO noted that procedures for making variants of SEQ ID NO:3 were conventional in the art (i.e., site specific mutagenesis) and that an activity assay was disclosed. It concluded that the claimed genus "does not have substantial variation since all the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence, SEQ ID NO:3".

Claim 2 requires that the ghrelin-like compound be at least 95% homologous to SEQ ID NO:1 and therefore clearly falls within the "safe haven" of WDTM Ex. 14. In this regard, we respectfully direct the Examiner's attention to the definition of "homology" at page 46, lines 11-22, and to the definition of a ghrelin-like

compound at page 12, lines 15-19. The term "ghelin-like compound" has an implicit functional dimension and assays for the recited functions (ghrelin receptor activation stimulation of appetite, inhibition of cachexia) are conventional, see Examples 4, 5, 7 and 11.

See also page 43, line 28 to page 46, line 7.

We recognize that in WDTM Ex. 14, the sample claim coupled the aforementioned structural (95% identity) limitation with a functional (enzymatic activity) limitation. The instant claim is a method-of-use claim and already requires administration of a "prophylactically or therapeutically effective amount...." If a compound meeting the structural limitation lacked the ability to provide "prophylaxis or treatment of cancer cachexia", no "effective amount" would exist and thus the compound would be implicitly excluded. However, to advance prosecution we have made this functionality explicit by adding "wherein said ghrelin-like compound or pharmaceutically acceptable salt thereof has prophylactic or therapeutic activity against cancer cachexia".

We have also added claims reciting relevant pharmacological activity limitations. Claim 46 is based on page 44, lines 5-7 and page 45, lines 14-15; claim 47 on page 45, lines 22-23, and claim 48 on page 45, lines 7-8.

With regard to claim 1, requiring (a) 80% homologous and 27-28 aa long, or (b) 90% homologous and no explicit fixed length (a minimum length is implied by the % homology requirement) , we respectfully urge that the lower percentage identity is (1) well within the range of % identity limitations permitted in the past by the PTO, and (2) justified by the disclosure of complete structures for several species and not just one species as in WDTM Ex. 14.

With regard to the first point, we respectfully direct the Examiner to the following exemplary patents:

Patent/claim	%
USP 5,304,640 claim 2	40%
Bell, USP 4,761,371 claim 8	40%
Holtzman 6,410,232	55%
Wang, 6,639,051 claim 17	60%
Yurchenko 6,632,790 claim 2	70%
USP 5,670,335	70%
USP 5,538,892	70%
Deeley, USP 5,489,519	70%
Tarczynski 6,372,961	70%
Stafford, USP 5,268,275 claim 13	75%
Hoffman, USP 5,545,727 claim 9	75%
Sheppard, 6,265,544	75%
Sheppard, 6,498,235	80%
Mahajan 6,388,169	80%
Williams, 6,642,022	80%
Friedman 6,429,290	83%
Hayden 6,617,122 claim 33	85%
Bertin, 6,482,933	85%
Sim 6,482,403	85%
Crabtree 6,388,052	90%
Raju 6,500,654 claim 10	90%
Acton 6,436,685	90%
Cerretti RE37,582	90%

The following cases illustrate the relevance of prior patents:

> Ex parte Brian, 118 USPQ 242, 245, (POBA 1958) (past practice of office in accepting definiteness of "fingerprint" claims);
> In re Chakrabary, 596 F.2d 952, 985-86 (CCPA 1979)

(product claims reciting microorganisms previously treated as directed to statutory subject matter);

Andrew Corp. v. Gabriel Electronics, Inc., 6 USPQ 2010, 2012 (Fed. Cir. 1988) (term "substantially" is "ubiquitous" in patent claims and therefore considered definite);

In re Cortright, 49 USPQ2d 1464 (Fed. Cir. 1999) (Construction of "restore hair growth" for purpose of determining both §112 enablement and §101 utility; prior art references may be indicative of how a claim term will be interpreted by those of ordinary skill in the art);

Vitronics Corp. v. Conceptronic Inc., 39 USPQ2d 1573, 1578-9 (Fed. Cir. 1996) (prior art used to demonstrate how a disputed term is used by those skilled in the art, and indeed is more objective and reliable than post-litigation expert opinion testimony);

Pioneer Hi-Bred International v. J.E.M. Ag Supply Inc., 49 USPQ2d 1813, 1819 (N.D. Iowa 1998) (issuance of Boehm USP 2,048,056 in 1936 is evidence that "in those instances where inventors showed they could define a reproducible plant meeting the limits of §112, plant patents were issued under §101".)

With regard to the second point, in Ex parte Gleave, 84 USPQ2d 1681 (BPAI 2006), the Board held that the disclosed mouse and human IGFBP sequences were representative of the claimed genus "mammalian". It is not, of course, unusual for the class of mammalian homologues of a human protein to include pairs whose percentage identity is as low as, or even lower than, 75%.

It is true that in Ex parte Kubin, 83 USPQ2d 1410 (BPAI 2007), claims to DNAs encoding proteins with at least 80% identity to human NAIL were held unrepresentative of the claimed genus. But there, (1) the disclosed DNAs encoded fusion proteins all of which comprised just the mature human NAIL sequence, without variation (i.e., insofar as the NAIL protein component was concerned, there was just a single complete structure), and (2) there was no guidance as to variation, e.g., identification

of binding sites.

Here, first of all, clause (b) of claim 1 requires a higher percentage identity (90%) than does Kubin. While clause (a) requires the same level, the claim is supported by three different complete structures, whereas the claim in Kubin was supported by only one.

Our SEQ ID NO:2 differs from SEQ ID NO:1 by deletion of Gln-13 from SID1 (about 96% identity). Our SEQ ID NO:3 differs from SEQ ID NO:1 by the substitutions R11K and V12A (about 93% identity).

In any event, even if the Examiner is unwilling to acknowledge written description for 80% identity, it should be acknowledged for the 90% identity of new claim 50, the 95% identity of claim 2 or the 98% of claim 3.

Moreover, new claim 49 deserves separate consideration. Claim 49 permits the ghrelin-like compound to differ in amino acid sequence from human ghrelin solely by (1) N- or C-terminal extensions (basis at page 46, line 16), (2) N- or C-terminal truncations (basis at page 39, line 17; page 40, line 6 to page 43, line 26), and (3) conservative amino acid substitutions (basis at page 47, line 21 to page 49, line 23). The permissible truncations are, as previously discussed, already limited by clauses (a) and (b); the ghrelin-like compound cannot be less than 25 a.a. and, since human ghrelin is 28 a.a., that means no more than three a.a. can be truncated.

The rejection notes that the claimed secretagogues can contain D-amino acids, beta-amino acids, gamma amino acids, and an amino acid modified with a bulky hydrophobic group. However, WDTM ex. 14 did not place any constraints on the nature of the amino acid substitutions made, other than the overall limitation on the total divergence. Replacement of an L-alpha amino acid with a D-amino acid or a beta amino acid would reduce the percent homology and only a limited number of such replacements is

permitted by even claim 1. New claim 49, it should be noted, does not permit replacement with D-amino acids, beta amino acids, or gamma amino acids, and see also new claims 51 and 52.

We note that there is a detailed disclosure concerning possible "bulky hydrophobic groups" at pages 50-52. We have specifically exemplified an N-acetylated ghrelin (1-10) at page 88, lines 13-15.

It should be noted that ghrelin in nature is an acylated peptide; the original sequence listing indicates that in SEQ ID NO:1, Ser-3 is modified with a fatty acid.

In conclusion, applicants have disclosed the complete structures of a representative number of species within the genus of claim 1 and consequently have written description for the genus of claim 1.

4. Enablement

Claims 1-3, 6, 13-20, 22-23, 27-29, 31, 33-35 and 37 stand rejected for allegedly insufficient enablement. The Examiner concedes that the specification is enabling for "treating" cancer cachexia but not for "preventing" cancer cachexia. The Examiner appears to make two arguments.

4.1. The first is that to prevent cancer cachexia, one must identify a patient subpopulation which is at risk of developing cancer cachexia. The Examiner then proclaims that since we can't say which individuals are susceptible to cancer, we don't know which ones are at risk of cancer cachexia.

Let us first point out that if a drug has a sufficiently high margin of safety, it could be administered to the entire population, thereby "preventing" the cancer cachexia, without making any effort to identify individuals at risk. The greater the margin of safety, the less need there is for accurate risk assessment.

The Examiner has not made any showing that ghrelin has a low

margin of safety and hence that risk assessment is critical.

Nor do we agree that the art fails to provide any guidance as to individuals who are susceptible to cancer. For example, it is well known that chronic smokers are susceptible to lung cancer. Likewise, genetic markers have been identified for several cancers, e.g., AMACR for prostate cancer (see Wong, Sci. Am. News, Apr. 3, 2002) and BRCA1 and 2 for breast and ovarian cancer, see USP 5,821,328.

Nonetheless, we have amended claim 1 to specify "wherein, for prophylaxis, the individual is one who is suffering from cancer", with basis at page 21, line 13. Since the individual is required to have cancer, the individual is clearly at risk of cancer cachexia. In this regard, note that the Examiner reads Brennan (1977) as teaching that "starvation" ("cancer cachexia") is a "common accompaniment to the presence of cancer" (OA p. 14) and Tisdale (2000) likewise recognizes that patients with cancer "often experience a life threatening muscle wasting syndrome known as cachexia", although Tisdale dislikes characterizing it as "starvation"). (OA p. 15). Note also the Examiner's use of "often coincides" in discussing the teachings of Illman (2005) (Id.) It therefore appears that the Examiner would agree that anti-cachexia prophylaxis is appropriate for the subpopulation of cancer patients generally.

A second criticism is made on page 23, second full paragraph:

> Please note that the term "prevent" as well as "prophylaxis" in an absolute definition which means to stop from occurring and, thus, requires a higher standard for enablement than does "therapeutic" or "treat" or "alleviate", especially since it is notoriously well accepted in the medical art that the vast majority of afflictions/disorders suffered by mankind cannot be totally prevented with current therapies (other than certain vaccination

> regimes)- including preventing such disorders as cancers and cancer cachexia, which is clearly not recognized in the medical art as being totally preventable condition.

The term "prevent" is not used in the claims, although it is used in the specification.

The Examiner fails to cite any authority for the proposition that the skilled worker would read "prevent" as requiring that cancer cachexia was prevented in every patient to whom it was administered. Because the "vast majority of afflictions/disorders suffered by mankind cannot be totally prevented with current therapies" (OA p. 23) it is unreasonable for the Examiner to infer that the skilled worker in the art would interpret "prevent" as requiring total prevention.

Moreover, it seems to use that if a drug is administered to 100 subjects who are thought sure (based on epidemiological data) to develop a disease, and the disease manifests itself in, say, 40 of them, then the drug indeed <u>prevented</u> the disease in the other 60. In other words, the evaluation as to whether absolute "prevention" occurred could reasonably be made on a subject-by-subject basis, rather than collectively.

In any event, the claims speak of "prophylaxis" rather than "prevention" of cachexia. The term "prophylaxis" is frequently used in patent claims, and there is basis for "prophylaxis" at page 5, line 6. We believe that "prophylaxis" as commonly used in the art encompasses partial prevention. The Examiner has made no showing to the contrary. Indeed, it is evident from P6, L1 that the purpose of the prophylaxis is to <u>lower the risk</u> of cancer cachexia and not necessarily to absolutely prevent it. To advance prosecution, claim 1 now recites that the prophylaxis lowers the risk of cancer cachexia, with basis at P6, L1.

5. Prior Art Issues

5.1. Claims 1-3, 6, 13-18, 20, 22, 27-29, 31, 33-35, 39-40 and 43-44 stand rejected as anticipated by Bednarek, WO 01/92292.

5.2.1. The first allegedly anticipatory species is human ghrelin. According to Bednarek, page 3, lines 14-16, human ghrelin is a 28 a.a. peptide in which Ser-3 is modified by acylation (with $-CO(CH_2)_6CH_3$) fo the hydroxyl side chain.

To anticipate, Bednarek must teach all aspects of the claim. The claim is not to ghrelin per se, but rather to the use of certain ghrelin-like compounds (which admittedly include human ghrelin) in the prophylaxis and treatment of cancer cachexia.

The first issue, then, is whether Bednarek adequately teaches use of ghrelin (as distinct from the truncated ghrelin analogs which he claimed) against cancer cachexia.

The potentially relevant disclosures by Bednarek appear to include:

1) "the present invention features truncated ghrelin analogs active at the GHS receptor" (P3, L6-7; P4, L32-33).

2) structure of human ghrelin (P3, L11-16; P4, L33-P5, l2). Ghrelin induces growth hormone release (P5, L3-5).

3) core region is first four AAs (P3, L18-20).

4) ghrelin analogues are useful as research tools and as therapeutic agents (P3, L8-10).

5) ghrelin analogues are useful for stimulating GH secretion (P4, L18-20).

6) ghrelin analogues can be used to screen for both ghrelin agonists and ghrelin antagonists (P5, L17-18).

7) ghrelin agonists can be used for "facilitating a weight gain", "facilitating maintenance of weight" and "facilitating appetite increase." (P5, L30-35). Latter is "particularly useful for patient having a disease or disorder, or undergoing a treatment, accompanied by weight loss." (P5, L35 - P6, L2). "Examples of diseases and disorders accompanied by weight loss include …… cancer cachexia ……." (P6, L2-3).

8) "The smaller size of truncated ghrelin analogs offers advantages over longer-length ghrelin such as ease of synthesis and/or increased solubility in physiological buffers."

The first sub-issue then is whether ghrelin per se qualifies as a ghrelin agonist per point 7, which is the only reference to cancer cachexia. For Bednarek to anticipate, it must be certain that Bednarek considered ghrelin to qualify.

According to the dictionary definition appearing at Meriam-Webster online, we have: "agonist: a chemical substance capable of combining with a specific receptor on a cell and initiating the same reaction or activity typically produced by the binding endogenous substance", implying that the agonist is not "the binding endogenous substance".

Likewise, Dorland's Illustrated Medical Dictionary defines "agonist" as "in pharmacology, a drug that has affinity for and stimulates physiologic activity at cell receptors normally stimulated by naturally occurring substances". The "drug" is thus differentiated from those "naturally occurring substances".

It is possible that other dictionary definitions can be found which would explicitly include the natural ligand in the class of "agonists" but even if that were the case, it would merely create uncertainty as to Bednarek's teachings and uncertainty is fatal to anticipation.

The second sub-issue is whether Bednarek is "enabling" for

use of ghrelin (as opposed to truncated ghrelin analogs). The potentially relevant disclosure is the section "Administration" on pages 14-16. This describes means for the administration of "truncated ghrelin analogs" rather than of "ghrelin agonists". The Examiner cannot properly rely on it for enablement of use of ghrelin because it clearly constitutes a part of the specification which relates only to ghrelin analogues (by definition, different from ghrelin). See In re Arkley, 172 USPQ 524 (CCPA 1972) (criticizing the "picking and choosing" of disparate teachings), and Daiichi Pharmaceutical Co. v. Apotex, Inc., 83 USPQ2d 1471 (D.N.J. 2006) (criticizing the combination of "unrelated" portions of the disclosure), reversed on other grounds (obviousness) without reaching the anticipation issue, 84 USPQ2d 1285 (Fed. Cir. 2007).

Hence, there are two reasons why Bednarek's teachings concerning human ghrelin cannot be considered anticipatory of the present method claim.

5.2.2. Bednarek also discloses certain truncated ghrelin analogs, which "have the structure Z^1-GSX1=$(Z)_n$-Z^2 or Z^1-GXSF$(Z)_n$-Z^2".

The Z^1 and Z^2 are protecting groups. GSXF or GXSF each constitute exactly four amino acids, X being "a modified amino acid containing a bulky hydrophobic R group". The Z's are the 20 genetically encoded amino acids, "or a derivative thereof". The n is restricted to 0-19, and hence the truncated ghrelin analogues have lengths of 4+"0-19", i.e., 4-23 amino acids.

The term "have", depending on context, can be "open" or "closed". Compare Scripps Research Institute v. Genentch, Inc., 77 USPQ2d 1809, 1819 (BPAI 2005) (non-precedential) with University of California v. Eli Lily & Co., 43 USPQ2d 1398, 1410 (Fed. Cir. 1997). The Scripps Board declared, "The transitional phrase 'has' can open up a limitation, but it does not convey openness as strongly as 'comprises' and, thus, does not create

a presumption that the limitation is open unless the count as a whole requires an open construction".

We argued that Bednarek's "have" or "having" (claim 1) must be interpreted as "closed" (can't add additional amino acids) because he teaches that "the smaller size of truncated ghrelin analogues offers advantages over longer-length ghrelin...", see page 6, lines 18-19.

At page 4 of the office action the Examiner argued that Bednarek does not teach that his truncated ghrelin analog structures are "closed", as evidenced, supposedly, by their failure to end in amide (sic, amino) at the N- or carboxyl at the C-terminal ends.

This argument, first of all, completely ignores the fact that the PTO instructs applicants not to show the terminal NH_2- and -COCH in a sequence identified by SEQ ID NO:. Thus, 37 CFR 1.822(d) says, "the amino and carboxy groups shall not be presented in the sequence".

Secondly, the terminal NH_2- and -COOH are recited in the structure on Bednarek page 6, specifically in the definitions of Z^1 and Z^2 at lines 32-35:

> Z1 is an optionally present protecting group that, if present, is covalently joined to the N-terminal amino group;
>
> Z2 is an optionally present protecting group that, if present, is covalently joined to the C-terminal carboxy group;....
> (emphasis added)

It follows that the "G" is the first amino acid and the nth "Z" the last amino acid of the recited sequences. Thus, Bednarek does not disclose ghrelin analogues longer than 23 a.a.

Our claim 1, paragraph (a) requires that the ghrelin-like compound be both at least 80% homologous to SEQ ID NO:1 (which, standing alone, since SID1 is 28 a.a., could read on a 23 a.a. fragment of SID 1) and that it be "27-28 amino acids in length"

(which excludes the 23 a.a. "option").

Paragraph (b) requires that it be at least 90% homologous, i.e., at least (nominally) "25.2" amino acids (and since a fraction makes no sense, that means at least 26 amino acids).

Both paragraphs (a) and (b) thus exclude Bednarek's truncated ghrelin analogs.

5.3. It should be noted that in an obviousness inquiry, it becomes relevant that Wisse, et al. (2001) teach away from the invention by disclosing that ghrelin is inefficient for stimulating food intake in tumor bearing rats (fig. 5 and page 3300, col. 1, first half).

5.4. Claim 37 is rejected (OA §§24-30) as obvious over Bednarek in view of Okamoto. Okamoto is cited merely to show administration of an NSAID (zaltoprogen) and does not remedy the deficiencies of Bednarek.

5.5. Claims 19 and 23 are rejected as obvious over Bednarek (OA §§31-35). These claims relate to the time of administration. However, this rejection does not address the issue that Bednarek advocates a more drastic truncation than that permitted by applicant's claim 1.

Respectfully submitted,

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